```
     (FILE 'USPAT' ENTERED AT 15:25:15 ON 05 AUG 95)
L1          5492 S PHOSPHOLIPID?
L2           278 S NEUTRAL LIPID?
L3           191 S L1 AND L2
L4          8563 S TRIGLYCERID?
L5          1094 S L1 AND L4
L6          1107 S PHOSPHATIDYLCHOLINE?
L7           208 S L4 AND L6
L8           132 S CHOLESTERYL ESTER
L9           136 S SPHINGOSINE
L10           12 S L7 AND L8
L11            4 S L7 AND L9
L12            0 S L10 AND L11
=>
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     (FILE 'USPAT' ENTERED AT 15:25:15 ON 05 AUG 95)
L1          5492 S PHOSPHOLIPID?
L2           278 S NEUTRAL LIPID?
L3           191 S L1 AND L2
L4          8563 S TRIGLYCERID?
L5          1094 S L1 AND L4
L6          1107 S PHOSPHATIDYLCHOLINE?
L7           208 S L4 AND L6
L8           132 S CHOLESTERYL ESTER
L9           136 S SPHINGOSINE
L10           12 S L7 AND L8
L11            4 S L7 AND L9
L12            0 S L10 AND L11
L13         2937 S LIPOSOM?
L14          286 S L13 AND L4
L15           77 S L14 AND L6
L16            5 S L15 AND L8
L17            1 S L15 AND L9
L18            0 S L16 NOT 10
L19            0 S L16 NOT L10
L20            0 S L17 NOT L11
L21           57 S L13 AND L9
L22            0 S L21 AND L8
L23            5 S L21 AND L4
=>
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(FILE 'HOME' ENTERED AT 15:57:02 ON 05 AUG 95)

FILE 'REGISTRY' ENTERED AT 15:57:07 ON 05 AUG 95

FILE 'CA' ENTERED AT 15:57:40 ON 05 AUG 95

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L1         30933 S PHOSPHATIDYLCHOLIN?
L2         32173 S TRIGLYCERID?
L3          2486 S CHOLESTERYL ESTER
L4          1932 S SPHINGOSIN?
L5          3659 S CHOLESTERYL ESTER?
L6          1603 S L1 AND L2
L7             4 S L6 AND L4
L8           121 S L6 AND L5
L9            64 S LIPSOM?
L10        23271 S LIPOSOM?
L11         7589 S L10 AND L1
L12           33 S L11 AND L2
L13           23 S L11 AND L4
L14           53 S L11 AND L5
L15            0 S L12 AND L13 AND L14
L16            0 S L12 AND L13
L17            0 S L13 AND L14
L18            8 S L12 AND L14

=>
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L13 ANSWER 10 OF 23 CA COPYRIGHT 1995 ACS
AN 110:5222 CA
TI Calcium-independent activation of prothrombin on membranes with positively charged lipids
AU Rosing, Jan; Tans, Guido; Speijer, Han; Zwaal, Robert F. A.
CS Dep. Biochem., Univ. Limburg, Maastricht, 6200 MD, Neth.
SO Biochemistry (1988), 27(25), 9048-55
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
OS CJACS
AB The activation of prothrombin by blood-coagulation factor Xa is strongly accelerated by neg. charged phospholipids plus Ca2+. Here, it is reported that pos. charged membranes can also stimulate prothrombin activation provided that the activation reaction is carried out in the absence of Ca2+. Membranes composed of a mixt. of ***phosphatidylcholine*** (PC) and pos. charged lipids like stearylamine, ***sphingosine*** , or hexadecyltrimethylammonium bromide caused a >1000-fold increase of the rate of prothrombin activation. Prothrombin activation by the factor Xa-factor Va complex was also considerably stimulated by such membranes. Stimulation of prothrombin activation by pos. charged membranes was suppressed at high ionic strength. This suggests that electrostatic attraction of neg. charged proteins by pos. charged membranes is the major driving force in the assocn. of prothrombin and factor Xa with the lipid surface. Ca2+ strongly inhibited prothrombin activation on vesicles composed of PC and stearylamine (80/20 M/M), which indicated that the .gamma.-carboxyglutamic acid (Glu)-contg. regions of prothrombin and/or factor Xa are important for the interaction of these proteins with pos. charged membranes. The importance of the Gla domain was confirmed by the observation that PC/stearylamine vesicles had much less effect on the reactions between proteins that lack Gla residues [Gla-domainless de-1-45-prothrombin, prethrombin 1, prethrombin 2, or Gla-domainless de-1-44-factor Xa]. The efficiency of prothrombin and prothrombin derivs. to act as substrate decreased in the order prothrombin > de-1-45-prothrombin = prethrombin 1 > prethrombin 2, whereas prothrombin activation by Gla-domainless de-1-44-factor Xa was hardly stimulated by pos. charged membranes. These results indicated that the main function of the Gla domain relates to a contribution of Gla to the overall neg. charge of the proteins. The findings further suggested that it is possible to form a fully active membrane-bound prothrombinase complex by pure electrostatic interactions and that the interaction of metal ions with Gla residues is no prerequisite for the expression of the catalytic activity of such a membrane-bound complex.

ST prothrombin activation pos charged membrane